Toxicology. 2000 Aug 7;148(2-3):187-97.

Free radicals and grape seed proanthocyanidin extract: importance in human health and disease prevention.

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Free radicals have been implicated in over a hundred disease conditions in humans, including arthritis, hemorrhagic shock, atherosclerosis, advancing age, ischemia and reperfusion injury of many organs, Alzheimer and Parkinson's disease, gastrointestinal dysfunctions, tumor promotion and carcinogenesis, and AIDS. Antioxidants are potent scavengers of free radicals and serve as inhibitors of neoplastic processes. A large number of synthetic and natural antioxidants have been demonstrated to induce beneficial effects on human health and disease prevention. However, the structure-activity relationship, bioavailability and therapeutic efficacy of the antioxidants differ extensively. Oligomeric proanthocyanidins, naturally occurring antioxidants widely available in fruits, vegetables, nuts, seeds, flowers and bark, have been reported to possess a broad spectrum of biological, pharmacological and therapeutic activities against free radicals and oxidative stress. We have assessed the concentration- or dose-dependent free radical scavenging ability of a novel IH636 grape seed proanthocyanidin extract (GSPE) both in vitro and in vivo models, and compared the free radical scavenging ability of GSPE with vitamins C, E and beta-carotene. These experiments demonstrated that GSPE is highly bioavailable and provides significantly greater protection against free radicals and free radical-induced lipid peroxidation and DNA damage than vitamins C, E and beta-carotene. GSPE was also shown to demonstrate cytotoxicity towards human breast, lung and gastric adenocarcinoma cells, while enhancing the growth and viability of normal human gastric mucosal cells. The comparative protective effects of GSPE, vitamins C and E were examined on tobacco-induced oxidative stress and apoptotic cell death in human oral keratinocytes. Oxidative tissue damage was determined by lipid peroxidation and DNA fragmentation, while apoptotic cell death was assessed by flow cytometry. GSPE provided significantly better protection as compared to vitamins C and E, singly and in combination. GSPE also demonstrated excellent protection against acetaminophen overdose-induced liver and kidney damage by regulating bcl-X(L) gene, DNA damage and presumably by reducing oxidative stress. GSPE demonstrated excellent protection against myocardial ischemia-reperfusion injury and myocardial infarction in rats. GSPE was also shown to upregulate bcl(2) gene and downregulate the oncogene c-myc. Topical application of GSPE enhances sun protection factor in human volunteers, as well as supplementation of GSPE ameliorates chronic pancreatitis in humans. These results demonstrate that GSPE provides excellent protection against oxidative stress and free radical-mediated tissue injury.